The use of an intra-oral injection of ketorolac in the treatment of irreversible pulpitis

A. C. Mellor[1], M. L. Dorman[2] & N. M. Girdler[3]

[1]School of Dentistry, The University of Manchester, Manchester; [2]Department of Oral and Maxillofacial Surgery, Sunderland Royal Hospital, Sunderland; and [3]School of Dental Sciences, University of Newcastle, Newcastle upon Tyne, UK

Abstract

Mellor AC, Dorman ML, Girdler NM. The use of an intra-oral injection of ketorolac in the treatment of irreversible pulpitis. *International Endodontic Journal*, **38**, 789–794, 2005.

Aim To examine whether an intra-oral injection of a nonsteroidal anti-inflammatory drug (ketorolac), in association with conventional local anaesthetic techniques, would improve the pulp extirpation rate in teeth with irreversible pulpitis.

Methodology A two group double-blind clinical trial was undertaken in the Dental Casualty Department of the University of Manchester School of Dentistry. Patients were randomly allocated to either the test or control group. The test group received an intra-oral injection of ketorolac (30 mg in 1 mL) in the buccal sulcus adjacent to the tooth being treated. After an interval of 15 min, they then received 2.2 mL of 2% lidocaine with 1 : 80 000 epinephrine by buccal infiltration in the maxilla or by inferior dental block in the mandible. The control group received an intra-oral injection of normal saline (1 mL) in the buccal sulcus adjacent to the tooth being treated, followed by the same local anaesthetic regime as the test group after the 15 min interval. Fifteen minutes after the local anaesthetic injections, pulp extirpation was attempted. All patients completed the short-form McGill pain questionnaire prior to treatment and completed identical questionnaires at 6 and 24 h after treatment.

Results The study protocol set the number of patients to be treated at twenty. However, as the study progressed it became apparent that the intra-oral injection of ketorolac caused significant pain to four of the five patients who received it; therefore the study was terminated after ten patients had been treated. The results from the patients treated showed no significant difference in the pulp extirpation rate between the test and control groups. However, patients with higher pain scores at baseline were less likely to have the pulp completely extirpated, irrespective of whether they were in the test or control group. Pain scores for all patients decreased significantly from baseline to 24 h.

Conclusion An intra-oral injection of ketorolac did not improve the pulp extirpation rate in a small group of patients with irreversible pulpitis compared with a placebo. In addition, it was associated with such significant pain on injection that it cannot be recommended as a treatment in this situation.

Keywords: dentistry – treatment, ketorolac, Nonsteroidal anti-inflammatory drugs, pulpitis – irreversible, pulpitis – treatment.

Received 24 February 2005; accepted 7 June 2005

Introduction

It is well recognized that in the presence of acute inflammation, conventional infiltration or block local anaesthetic injections may not achieve complete anaesthesia. In teeth with irreversible pulpitis, this means that total removal of the dental pulp is not always possible because the patient feels pain. In these situations, a sedative dressing, such as the corticosteroid/antibiotic mixture Ledermix®, (Blackwell Supplies, Gillingham, UK) is often applied to the inflamed pulp and pulp removal completed at a subsequent visit (Stock *et al.* 2004).

Correspondence: Dr A. C. Mellor, School of Dentistry, The University of Manchester, Higher Cambridge Street, Manchester M15 6FH, UK (Tel.: +44 (0) 161 275 6729; fax: +44 (0) 161 275 6299; e-mail: tony.mellor@manchester.ac.uk).

Supplementary local anaesthetic techniques to aid removal of the inflamed pulp, such as intra-ligamentary (Edwards & Head 1989), intra-osseous (Nusstein *et al.* 1998, Parente *et al.* 1998) or even intra-pulpal injections (Teixera *et al.* 2001), are often painful and are not always effective.

An alternative approach would be to try to reduce the inflammation directly. If complete pulpal anaesthesia could be achieved and the pulp removed in one visit, this would give more rapid pain relief for patients and considerably reduce the time spent on emergency primary dental care. Inflammation alters the response properties of nociceptors through the action of inflammatory mediators such as prostaglandins. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ketorolac (Buckley & Brogden 1990) are potent inhibitors of prostaglandin synthesis but have mainly been dispensed as oral tablets or by intra-muscular injection. Ketorolac has been administered by intra-oral injection for endodontic pain (Penniston & Hargreaves 1996) and it has also been used as an intra-canal medicament in endodontics (Rogers *et al.* 1999).

A small study was designed which aimed to determine whether an intra-oral injection of an NSAID (ketorolac) would have a sufficient anti-inflammatory effect to allow conventional local anaesthetic injections to completely anaesthetize teeth with irreversible pulpitis so that pulp removal could be achieved.

Materials and methods

Ethical approval for the study was granted by the Central Manchester Local Research Ethics Committee. The study was planned to be a two-group double-blind clinical trial. All the treatment was carried out by one operator (A.C. Mellor). The patient sample was selected from patients attending the Dental Casualty Department of the University Dental Hospital of Manchester.

The plan was to recruit twenty patients, with ten being randomly allocated to the test group and ten to the control group. The randomization was carried out using random number tables.

The inclusion criteria were:

- Patient aged between 18 and 65 years
- Diagnosis of irreversible pulpitis following clinical and radiographic examination, including vitality testing
- Patient requested pulp extirpation
- Patient able to read and understand questionnaires
- Patient able to give informed consent

The exclusion criteria were:

- History of allergy to NSAIDs, aspirin or local anaesthetics
- History of peptic ulceration, active asthma, decreased renal or liver function
- Currently taking diuretics or anti-coagulants
- Pregnant or nursing mothers

All patient were given an information sheet on the study prior to signing a consent form and then completed the short-form McGill pain questionnaire (Melzack 1987).

Treatment procedure

Topical lidocaine local anaesthetic cream (Lignocaine ointment 5%; Biorex Ltd, Enfield, UK) was placed at the injection site on a cotton wool roll for 2 min for all patients prior to the injection of ketorolac or a placebo (saline).

The test group received an intra-oral injection of ketorolac (30 mg in 1 mL) in the buccal sulcus adjacent to the tooth being treated. After an interval of 15 min, they then received 2.2 mL of 2% lidocaine with 1 : 80 000 epinephrine (Xylocaine; Dentsply) by buccal infiltration in the maxilla or by inferior dental block in the mandible.

The control group received an intra-oral injection of normal saline (1 mL) in the buccal sulcus adjacent to the tooth being treated, followed by the same local anaesthetic regime as the test group after the 15-min interval.

The ketorolac and the saline were both drawn up by one of the dental nursing staff in identical 2 mL disposable syringes with a 23-gauge needle. The operator was blind to which solution was in the syringe for each patient until after the treatment was completed and the patient had left the hospital.

Fifteen minutes after the local anaesthetic injections, pulp extirpation was attempted. At the completion of the extirpation or the treatment, the tooth was temporarily restored with Ledermix® Lederle paste, a dry cotton wool pledget and a temporary restoration (Poly F Plus; Dentsply).

Results

Ten patients were treated initially. Three female and two male patients had been allocated to each treatment. At that stage it became apparent to the operator that the injection of ketorolac or saline had caused considerable local discomfort for four patients, all of whom were subsequently found to have received

Table 1 Mean pain scores at baseline from the short form McGill pain questionnaire for the test and control groups

	Possible range	Group	*n*	Mean (SD)
Sensory score	0–33	Test	5	12.20 (5.54)
		Control	5	11.20 (7.22)
Affective score	0–12	Test	5	4.20 (2.78)
		Control	5	4.20 (2.78)
Total score	0–45	Test	5	16.40 (8.17)
		Control	5	15.40 (9.45)
VAS score	0–10	Test	5	5.84 (2.06)
		Control	5	5.68 (1.72)
VeAS score	0–3	Test	5	2.40 (0.55)
		Control	5	2.00 (0.71)

ketorolac. No patients who received the saline injection complained of discomfort in the region of the injection. It was therefore decided to discontinue the study at that stage and to examine the results for those patients treated.

The patients' ages ranged from 19 to 52 years, with similar means in the test and control groups (32.2 and 36.6 years). Baseline McGill pain scores for the test and control groups were similar (Table 1).

Extirpation of the pulp

In six teeth (60%) the pulp was completely extirpated. The pulp in the other four teeth (40%) was only partially extirpated because the patient could feel pain on instrumentation in either the pulp chamber or root canal. Extirpation was incomplete in three (60%) of five test teeth and one (20%) of five control teeth (relative risk 3, 95%; CI, 0.58–19.4) (Mietinnen & Nurminen 1985). Complete or partial pulp extirpation was not significantly different in maxillary or mandibular teeth ($P = 0.88$) or in pre-molar or molar ($P = 0.88$). Neither the gender of the patient ($P = 0.57$) nor the age of the patient ($P = 0.88$) were significant factors in whether the pulp could be fully extirpated.

Table 2 Mean pain scores at baseline from the short form McGill pain questionnaire for subjects who had the pulp either partially or completely extirpated

	Possible range	Extirpation	*n*	Mean (SD)	*P*
Sensory score	0–33	Partial	4	16.25 (3.40)	0.045
		Complete	6	8.67 (5.68)	
Affective score	0–12	Partial	4	6.00 (0.82)	0.07
		Complete	6	3.00 (2.76)	
Total score	0–45	Partial	4	22.25 (3.86)	0.04
		Complete	6	11.67 (7.92)	
VAS score	0–10	Partial	4	6.68 (0.99)	0.20
		Complete	6	5.15 (2.01)	
VeAS score	0–3	Partial	4	2.25 (0.50)	0.85
		Complete	6	2.17 (0.75)	

The mean total pain score at baseline was twice as high in subjects with partial compared with complete extirpation (Table 2). This difference applied to both the major sensory and the minor affective component, reaching statistical significance only for the former. The visual and verbal analogue scales did not differ significantly.

Discussion

The study was terminated early because of the pain associated with the intra-oral injection of ketorolac and because the ketorolac injection did not improve the pulp extirpation rate. Injection pain was not anticipated as a significant problem when the study was started. In previous work, it had been reported that 11 of 18 patients (61%) had transient pain after the intra-oral ketorolac injection (Penniston & Hargreaves 1996). The pain was described as brief and lasted for approximately 3–5 min. This was not the experience in this study. Patients complained of significant pain that was not transient. In the maxilla, the pain was eliminated when the local anaesthetic was injected but this was not the case in the mandible, as the inferior dental block did not cover the area where the injection had been given. Patient acceptability is a key factor in any new technique and if significant pain is a likely outcome, then acceptability is likely to be low.

Penniston & Hargreaves (1996) had no explanation of the pain following the intra-oral injection of ketorolac as an intramuscular injection of ketorolac did not have this side effect. They suggested giving local anaesthetic in the area of the injection before administering the ketorolac as a method of getting over this problem. This would be applicable in the maxilla but not in the mandible where a long buccal block would be needed in addition to the inferior dental block to anaesthetize the area of any injection in the molar region. There are ethical considerations in the giving of additional injections in addition to those that are clinically necessary.

In addition, this concept seems to be contradictory as the point of giving the ketorolac is to try to make the local anaesthetic more effective. To have to give a local anaesthetic first just to make the ketorolac injection

acceptable would only be acceptable practice if the ketorolac injection actually produced some clinical benefit. In this small sample, the complete extirpation rate was lower in the ketorolac group than in the saline group and therefore no further work with this drug regime is planned by the authors.

The fact that incomplete extirpation of the pulp was associated with higher McGill pain scores at baseline is interesting and could indicate further areas of study. Regular patients in general dental practice will be well known to the dentist in terms of their level of trait anxiety and treatment can therefore be adjusted to compensate for this. In a hospital or emergency situation, the dentist will not know the patient's level of trait anxiety or have any objective measure of their level of pain. From previous research it appears that few practitioners use dental anxiety questionnaires in their assessment of patients (Dailey *et al.* 2001). Pain questionnaires are not routinely used either but would seem to be of benefit in trying to identify potentially difficult patients to treat in an emergency situation.

Conclusions

The use of an intra-oral injection of ketorolac in the treatment of patients with irreversible pulpitis did not give any benefit in comparison with a placebo. In addition, the injection itself produced significant local discomfort in four of the five patients who received it. Because of this, the study was stopped early and the technique used here cannot be recommended as a treatment in this situation.

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COMMENTARY

The use of an intra-oral injection of ketorolac in the treatment of irreversible pulpitis – comment

The decision whether to publish the paper submitted by Mellor, Dorman and Girdler was a difficult one. A key requirement of the CONSORT guidelines for the reporting of clinical trials, which the journal has adopted, relates to adequacy and justification of sample size. The study as planned was very small and, had it completed as originally intended, might well have been judged unacceptable on these grounds. In the event, it was terminated pre-maturely because of unacceptability of the active treatment. This resulted in a still lower sample size, quite insufficient to support normal comparative analyses of efficacy.

Nevertheless we considered that it would be unethical to withhold publishing the conclusion that an